

Opioids
الأفيونات

المكثفات القوية

1- Strong analgesics

- Alfentanyl
- Fentanyl
- Heroin
- Meperidine
- Methadone
- Oxycodone
- Remifentanyl
- Sulfentanyl

المضادات الفينيه
والموسطه

2- Moderate / low analgesics

- Codeine

• Propoxyphene

3- Mixed agonist-antagonists
& partial agonists:
المضادات المضاهيات
المختلطة والمضاهيات
الجزئية

- Buprenorphine
- Butorphanol
- Nalbuphine
- Pentazocine

المضادات

4- Antagonists

- Nalmefene
- Naloxone
- Naltrexone

المكثفات الأخرى

5- other analgesics
• Tramadol

Pain

1- acute } Neurochemical process
 2- chronic }

{ site = - peripheral } subjective } → patient
 - central - CNS } description } (perception)
 بيان الحساسية

- Natural = morphine = juice - opium poppy =

- Synthetic = meperidine (pethadine)

uses 1 - therapeutic

- abuse

Mechanism of action: OPIOID Receptors

1- Mimic the action of endogenous peptide Neurotransmitters

- e.g. endorphins
- enkephalins
- dynorphins

2- interact with specific receptors :-

- μ (mu) receptors
- κ (kappa) receptors
- δ (delta) receptors

G-protein-coupled receptors family:

(18)

1- inhibit adenylyl cyclase enzyme

2- associated with ion channels →

• K^+ channels → ↑ efflux of K^+

① postsynaptic membrane
ions → membrane hyperpolarization
↓ glutamate excitatory response

• reducing postsynaptic presynaptic membrane Ca^{++} ion influx →

② presynaptic membrane

↓ neuronal firing & neurotransmitter

release (glutamate)

excitatory

neurotransmitter.

Receptors sites

1- CNS: Brain stem → RC.

cough C-

• CTZ → nausea vomiting
vomiting center

• CVS → blood pressure

• optic III N. C.

pupillary Diameter

• stomach secretions.

• thalamus - deep pain

• emotions.

• spinal cord: incoming sensory information

• Hypothalamus: - endocrine secretion

• limbic system: العواطف; العواطف → emotional behavior

2- peripheral NS:

- sensory N. fibers & terminals
- ↓ Ca⁺⁺ ion ~~release~~ dependent
- release of glutamate (↓ release)
- ↓ proinflammatory substances (subst P.)

3- immune cells: response or sensitivity } to painful stimuli

4- other organs . eg. gastrointestinal tract .
 . urinary bladder

pharmacological actions

1- Analgesic actions:

- acute
- chronic → tolerance
- severe pain:
 - angina pectoris → MS
 - fractures - femur.
Not head injury
- surgery
- burns.
- Cancer

2- euphoria - frontal lobe

3- R.C. ↓

4- ↓ cough centre.

- No tolerance

5- Miosis

- No tolerance

6- emesis CTZ, vomiting centre.

7- GIT - constipation - No tolerance

↓ mobility. ↓ secretion → antiperistalsis
↑ sphincter contraction → antiperistalsis

8- CVS → No significant effect

9- Histamine release - M.D. → bronchoconstriction
- M.D. cells. → mottles, sweating

10. Hormones

- ↓ release of gonadotropin-releasing H.
- ↓ corticotropin-releasing H.

• LH ↑

• FSH ↑

• Adrenocorticoids ↓

etc.

11. Labour:

- ↑ second labour stage

↓ strength

↓ duration

↓ frequency

uterine contraction

therapeutic uses:

- Analgesic

- diarrhoea

- cough

- pulmonary oedema

Adverse effects

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Chronic admin

Tolerance & physical dependence: withdrawal reaction

- repeated prolonged use
- RC: depression
- analgesia
- euphoria
- sedation

- doesn't develop to
- pupil - contraction
- constipation

Withdrawal reaction:

- Autonomic NS. ↑
- motor system
- psychological reaction: sweating
- Tremors → seizures → MS. spasm ... }
coma → death.

Stress reaction

- tachycardia, anxiety
- palpitation, insomnia
- GI disturbance
- Nausea
- vomiting

Drug craving:

شکر و غیره
افسردگی
خستگی

- cross-tolerance with other opioids.

2 Acute overdose

- anxiety
 - tremors
 - Muscle twitch.
 - convulsions
- head injury ~~*~~ entour indications

CNS → toxic metabolites

C.V.S = severe hypotension → after surgery.

endocrine: adrenal insufficiency { increased synt.

system: Myxedema

GI = dry mouth

- Nausea
- vomiting
- constipation
- biliary tract → cont. Surgery
- liver failure?

eye: Miosis
• blurred vision

urinary tract: urine retention.
Prostate?

R.T: bronchoconstriction asthma
• R.C. depression - death.

3- Drug interactions.

- MAOI → severe reaction → convulsion, hyperthermia
- other CNS depressants - r.d. alcohol.

pharmacokinetics

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Administration:

- Absorption from GIT: Morphine
 - Slow & erratic
 - codeine
 - Well absorbed
 - significant first-pass effect.

oral absorption:

in liver:

- SC, IM, IV

في طريقه الى الطور الثاني
more ~~reliable~~ reliable response

body tissues

- Distribution = All body tissues
- CNS - Blood Brain ^{barriers}
- fetuses → Not in labor?

- Fate = liver
- Conjugation + glucuronic acid

po

- urine
- small amount bile?

- Duration of action = 4 - 6 hours.